

C-7 the pharmaceutical composition of claim 13 to a patient in need thereof.--

REMARKS

The Examiner is respectfully requested to enter this Reply After Final in that it raises no new issues. Alternatively, the Examiner is respectfully requested to enter this Reply After Final in that it places the application in better form for Appeal.

Status of the Claims

Claims 1-16, 24-26, 32 and 33 are currently pending in the above-identified application. Claims 22 and 23 have been canceled. Claim 33 has been added. Claim 33 is similar in scope to original claim 26, except that claim 26 is directed to treating and ameliorating and claim 33 is directed to prevention. As such, no new matter has been added. Claims 1, 8, 9, 13, 15 and 32 have been amended to further define the heteroaryl. Inherent support is found at page 31, third paragraph. Claims 1, 8, 13, 15 and 32 have also been amended to define cycloalkyl as C₃₋₈ cycloalkyl. Support is found at page 31, last paragraph. Claims 7 and 10 have been amended to delete "as defined above". Claims 9, 15 and 32 have been amended to define the amide group. Support is found at page 32, first paragraph. Claim 24-26 have been amended to delete "preventing". Claims 1, 13, 15 and 32 have been amended to limit the claimed compound to exclude compounds disclosed in the prior

art. Applicants submit that no new matter has been added by the above claim amendments. Applicants also submit that no new issues are raised. As such, Applicants respectfully request the entry of the above claim amendments.

Rejections under 35 USC 112, second paragraph

The Examiner rejects claims 1-16, 22-26 and 32 as indefinite for the following reasons:

- (iii) The term "substituted" to define particular substituent compounds. Applicants amend the specification to recite "include" and delete "including, but not limited to". As such, one of ordinary skill in the art can determine which substituents are intended and the rejection should be withdrawn.
- (iv) The term "heteroaryl", without defining the number of carbon atoms, rings or heteroatoms. Applicants amend the claims to define the heteroaryl group as formed from one or more 5 or 6 membered rings that may contain 1 to 4 heteroatoms. As such, the rejection should be withdrawn.
- (v) The term "optionally substituted amide group". Applicants amend the claims to define the amide group as $\text{-CO-N(R}_a\text{)R}_b$, wherein R_a and R_b are hydrogen or C_{1-6} alkyl group. As such, the rejection should be withdrawn.

- (vi) The term "cycloalkyl" does not recite the number of carbon atoms. Applicants amend the claims to recite "C₃-C₈ cycloalkyl". As such, the rejection should be withdrawn.
- (vii) It is not clear which diseases are treated with the method of claims 22 and 23. Applicants submit that it is not necessary for Applicants to recite the specific diseases to be treated because the mechanism of treatment is recited and all diseases which respond to the recited mechanism would be encompassed by the claimed method. However, Applicants cancel claims 22 and 23 without prejudice to or disclaimer of the subject matter contained therein.

As Applicants have addressed and overcome all indefiniteness rejections, Applicants respectfully request that the rejections be withdrawn.

Rejection under 35 USC 112, first paragraph

The Examiner rejects claims 22-26 as not enabled by the disclosure of "preventing, treating and ameliorating" the recited diseases. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Applicants cancel claims 22 and 23; thus, the rejection is moot to these claims. Claims 24-26 have been amended to delete

"preventing". Clearly support for treating and ameliorating is found at page 107, last paragraph to page 115. Applicants have shown the reduction of infarct loci in the cerebral cortex of the rat population given the claimed compound. Moreover, Applicants submit that "K. Kawaguchi et al., Brain Research, 753, pp. 152-156 (1997)" shows a possible prevention of epilepsy to support Applicants' claim that the claimed compound can prevent diseases such as epilepsy. As such, the rejection should be withdrawn.

Information Disclosure Statement (IDS)

The Examiner requests that the compounds that are excluded by the original provision be disclosed. Applicants point to page 29, lines 10 and 11 of the specification where US Patents 4,670,555 and 4,782,066 are mentioned. The excluded compounds are disclosed in these patents. U.S. Patent 4,670,555 is already of record. U.S. Patent 4,782,066 is a divisional of U.S. Patent 4,670,555. A copy of U.S. Patent 4,782,066 is attached. As such, Applicants have fulfilled the duty of disclosure and the objection should be withdrawn.

Differences Between the Independent Claims

The Examiner requests an explanation of the differences between the independent claims. Applicants submit the following:

Claim 1. Generic genus of invented compound

Claim 13. Generic genus of pharmaceutical composition (Claim 1 plus a pharmaceutical carrier.

Claim 15. Subgenus of pharmaceutical preparation.

Claim 32. Subgenus of the compound of claim 1.

As such, Applicants submit that the independent claims have different scopes.

Rejections under 35 USC 102(b)

The Examiner rejects claim 1 as anticipated by Soliman et al., Badr et al., Dekeyser et al., El-Gendy et al. and Matsubara et al. Applicants traverse the rejection and respectfully request the withdrawal thereof.

Applicants amend claim 1 to exclude the compounds disclosed in Soliman et al., Badr et al. and Matsubara et al. Please see the proviso in claims 1, 13, 15 and 32 which limits the combination of A and R¹ and R². As such, Applicants submit that the presently claimed invention is not anticipated by Soliman et al., Badr et al. and Matsubara et al. and the rejection should be withdrawn.

Regarding Dekeyser et al., Applicants submit that the original proviso excludes the compounds disclosure in Dekeyser et al. Please see the specification at page 29, lines 10 and 11. As such, the rejection should be withdrawn.

Regarding El-Gendy et al., Applicants submit that in order for El-Gendy et al. to anticipate the present invention, R¹ would have

to be imide, which is not the case in the present invention. As such, El-Gendy et al. does not anticipate and the rejection should be withdrawn.

Conclusion

As Applicants have addressed and overcome all rejections in the Office Action, Applicants respectfully request that the rejections be withdrawn and that the claims be allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kecia Reynolds (Reg. No. 47,021) at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.


Pursuant to the provisions of 37 C.F.R. § 1.17 and 1.136(a), Applicants hereby petition for an extension of one (1) month to November 27, 2002 for the period in which to file a response to the outstanding Office Action. The required fee of \$110.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any

overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachments: Version with Markings to Show Changes Made
U.S. Patent 4,782,666
K. Kawaguchi, Brain Research, 753, 152-156 (1997)

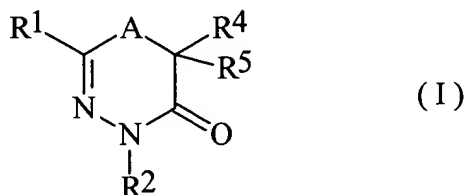
(Rev. 02/20/02)

VERSION WITH MARKINGS TO SHOW CHANGES MADEIN THE CLAIMS:

Claims 22 and 23 have been canceled.

The claims have been amended as follows:

1. (Amended) A compound represented by the following formula (I), a pharmacologically acceptable salt thereof or hydrates thereof:

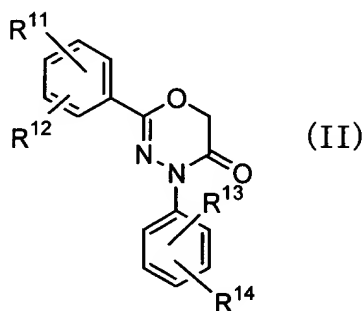


wherein A represents oxygen, sulfur or a group represented by the formula $>NR^3$ (wherein R^3 represents hydrogen atom or a lower alkyl group); R^1 represents an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed from one or two 5-6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group, an optionally substituted heteroaryl alkyl group, an optionally substituted aryl alkenyl group, an optionally substituted heteroaryl alkenyl group, an optionally substituted piperidyl group, an optionally substituted piperazinyl group, a morpholinyl group, an optionally substituted lower C_{3-8} cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an adamantyl group, an optionally substituted amino group

or an optionally substituted amide group that is $-\text{CO}-\text{N}(\text{R}_a)\text{R}_b$,
wherein R_a and R_b are hydrogen and C_{1-6} allyl groups; R^2
represents an optionally substituted aryl group, an optionally
substituted heteroaryl group that is formed from one or two 5-6
membered rings that may contain from 1 to 4 heteroatoms, an
optionally substituted aryl alkenyl group, an optionally
substituted heteroaryl alkenyl group, an optionally substituted
piperidyl group, an optionally substituted piperazinyl group, a
morpholinyl group, an optionally substituted lower C_{3-8}
cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl
group, an adamantyl group, an optionally substituted amino group
or an optionally substituted amide group that is $-\text{CO}-\text{N}(\text{R}_a)\text{R}_b$,
wherein R_a and R_b are hydrogen and C_{1-6} allyl group; and R^4 and R^5
are the same as or different from each other and each represents
hydrogen atom, hydroxyl group, nitrile group, nitro group, a
lower alkyl group, an aryl group or a heteroaryl group that is
formed from one or two 5 or 6 membered rings that may contain
from 1 to 4 heteroatoms,
provided that A is an oxygen atom, when R^1 and R^2 are both
phenyl; and
when A is a sulfur atom, R^1 is
an aryl which may have a substituent,
a heteroaryl which may have a substituent that is formed from
one or two 5-6 membered rings that may contain 1-4 heteroatoms,

an aralkyl which may have a substituent,
a heteroarylalkyl which may have a substituent,
an arylalkenyl which may have a substituent,
a heteroarylalkenyl which may have a substituent,
a piperidyl which may have a substituent,
a piperadinyll which may have a substituent,
a morpholinyl which may have a substituent,
a lower C₃₋₈ cycloalkyl which may have a substituent,
tetrahydrofuranyl,
adamantyl or
an optionally substituted amide, that is -CO-N(R_a)R_b, wherein R_a
and R_b are hydrogen and C₁₋₆ alkyl group; and

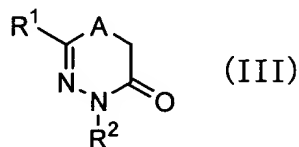
provided that the compounds represented by the following formula (II):



(wherein R¹¹ and R¹² are the same as or different from each other and each represents hydrogen atom, fluorine, chlorine, bromine, iodine, a C1-C2 fluoroalkyl group, a C1-C2 chloroalkyl group, a C1-C2 bromoalkyl group, a C1-C6 alkyl group, a C3-C6 cycloalkyl group, a C7-C9 aralkyl group, phenyl group, a C1-C6 alkoxy

group, a C1-C6 alkylthio group, a C1-C6 alkylsulfinyl group, a C7-C9 aralkoxy group, phenoxy group, phenylthio group, phenylsulfonyl group, an alkali metal carboxylate C2-C5 alkoxycarbonyl group or a group represented by the formula -N(R¹⁵)R¹⁶ (wherein R¹⁵ and R¹⁶ are the same as or different from each other and each represents hydrogen atom or a C1-C2 alkyl group); and R¹³ and R¹⁴ are the same as or different from each other and each represents a C₁₋₄ alkylsulfonyl group, nitro group, a group represented by the formula -OCH_nX_{3-n} (wherein X represents fluorine, chlorine, bromine or iodine; and n is an integer of 1 to 3) or the same groups as defined above for R¹¹ and R¹²) are excluded.

7. (Amended) The compound according to claim 1, wherein R⁴ and R⁵ are hydrogen and which is represented by the following formula (III):



(wherein A, R¹ and R² have the same meanings as defined in claim 1 [above]), a pharmacologically acceptable salt thereof or hydrates thereof.

8. (Amended) The compound according to claim 7, a pharmacologically acceptable salt thereof or hydrates thereof, wherein R^1 is an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group, an optionally substituted heteroaryl alkyl group, an optionally substituted aryl alkenyl group, an optionally substituted heteroaryl alkenyl group, a morpholinyl group, a lower C_{3-8} cycloalkyl group, an optionally substituted amino group or an optically substituted amide group that is $CO-N(R_a)R_b$, wherein R_a and R_b are hydrogen and C_{1-6} alkyl group; and R^2 is an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group, an optionally substituted heteroaryl alkyl group, a lower C_{3-8} cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an optionally substituted piperidyl group or an adamantyl group.

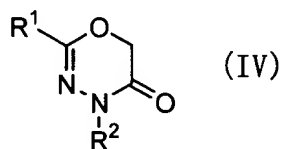
9. (Amended) The compound according to claim 7 or 8, a pharmacologically acceptable salt thereof or hydrates thereof, wherein the substituent groups on R^1 and R^2 are hydrogen atom, halogen atom, hydroxyl group, lower alkyl group, lower alkenyl

group, lower alkynyl group, lower alkoxy group, lower thioalkoxy group, hydroxy lower thioalkoxy group, arylthio group, heteroaryl thio group, heteroaryl(hydroxy)alkyl group, halogenated lower alkyl group, hydroxy lower alkyl group, dihydroxy lower alkyl group, halogenated (hydroxy) lower alkyl group, hydroxyalkenyl group, hydroxyalkynyl group, hydroxy lower cycloalkenyl group, lower alkoxy(hydroxy)alkyl group, lower alkoxy(hydroxy)alkoxy group, lower alkoxy alkyl group, lower alkoxy alkoxy group, lower thioalkoxy alkoxy group, lower alkyl sulfonyl alkoxy group, hydroxy lower alkoxy group, dihydroxy lower alkoxy group, hydroxy lower alkyl alkoxy group, hydroxy imino lower alkyl group, lower cycloalkyl(hydroxy)alkyl group, aralkyl group, hydroxyaralkyl group, cyano group, cyano lower alkyl group, amide group that is $-\text{CO}-\text{N}(\text{R}_a)\text{R}_b$, wherein R_a and R_b are hydrogen or C_{1-6} alkyl group, N-lower alkyl amide group, N-lower cycloalkyl amide group, N,N-di-lower alkyl amide group, N-hydroxy lower alkyl amide group, N-hydroxy lower alkyl-N-lower alkyl amide group, N-aryl amide group, cyclic aminocarbonyl group, carbamoyl group, N-lower alkyl carbamoyl group, N,N-di-lower alkyl carbamoyl group, aminosulfonyl group, cyclic aminosulfonyl group, N-lower alkyl aminosulfonyl group, N-lower cycloalkyl aminosulfonyl group, N,N-di-lower alkyl aminosulfonyl group, N-hydroxy lower alkyl aminosulfonyl group, N-lower alkoxy alkyl aminosulfonyl group, N-halogenated lower alkyl sulfonyl

group, pyrrolidinyl sulfonyl group, lower alkyl sulfonyl amino alkyl group, N-lower alkyl aminosulfonyl alkyl group, N,N-di-lower alkyl aminosulfonyl alkyl group, lower acyl group, lower acyl alkyl group, lower cycloalkyl(hydroxy)methyl group, tetrahydropyranyl group, hydroxytetrahydropyranyl group, hydroxy lower alkyl tetrahydropyranyl group, lower acyl amino alkyl group, (thiazole-2-yl)hydroxymethyl group, di(thiazole-2-yl)hydroxymethyl group, lower alkyl sulfonyl group, lower alkoxy alkyl sulfonyl group, hydroxy lower alkyl sulfonyl group, lower alkyl sulfonyl alkyl group, N-lower alkyl amide alkyl group, aryl group, aralkyl group, heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms, heteroaryl lower alkyl group, heteroaryl lower alkoxy group, heteroaryl sulfonyl group, 4-morpholinyl sulfonyl group, 4-oxythiomorpholinyl sulfonyl group, 4-dioxythiomorpholinyl sulfonyl group, 4-morpholinyl sulfonyl group, hydroxy lower cycloalkyl group, hydroxy lower cycloalkyloxy group, hydroxy cycloalkenyl group, halogenated hydroxy lower alkyl group, 4-hydroxypiperidyl group, 4-lower alkoxypiperidyl group, ω,ω -lower alkylene dioxyalkyl group, ω,ω -lower alkylene dioxy alkoxy group, lower cycloalkyl hydroxy methyl group, aryloxy group, aryl aminosulfonyl group, amino group, lower alkyl amino group, di-lower alkyl amino group, hydroxy lower alkyl amino group, lower acyl amino group, hydroxy

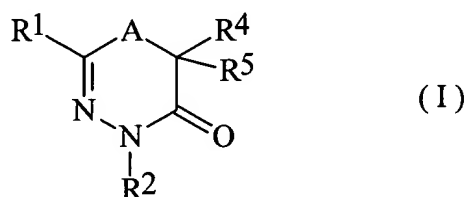
lower acyl amino group, lower alkyl sulfonyl amino group, pyridyl lower alkoxy group, lower alkyl pyridyl alkoxy group, lower alkoxy hydroxy alkoxy group, lower thioalkoxy alkoxy group, lower alkyl sulfonyl alkoxy group, N-lower alkyl carbamoyl group, N,N-di-lower alkyl carbamoyl group, N-hydroxy lower alkyl carbamoyl group, N-hydroxy lower alkyl-N-lower alkyl carbamoyl group, halogenated lower alkoxy group, cyano lower alkoxy group, hydroxy lower cycloalkoxy group, trifluoromethyl group, trifluoromethoxy group, amino lower alkoxy group, N-lower alkyl aminoalkoxy group, N,N-di-lower alkyl aminoalkoxy group, lower acyl alkoxy group, lower acyl aminoalkoxy group, (1,3-dioxolanyl) lower alkyl group, (1,3-dioxolanyl) lower alkoxy group, amide lower alkoxy group, 4-(hydroxy alkyl)tetrahydropyran-4-yl group, 2,3-dihydrobenzofuranyl group, 2-hydroxy-2-alkyl-2,3-dihydrobenzofuranyl group, indanonyl group, hydroxyindanyl group, imidazolyl lower alkoxy group, succimide group or 2-oxazolidone-3-yl group, optionally substituted benzoyloxy lower alkyl group, optionally substituted amino lower alkyl group, optionally substituted amino lower alkoxy group, optionally substituted aralkyloxy group, optionally substituted heteroaryl alkoxy group, optionally substituted morpholinyl lower alkoxy group, optionally substituted piperidyl lower alkoxy group, optionally substituted piperazinyl lower alkoxy group or optionally substituted pyrrolidinyl lower alkoxy group.

10. (Amended) The compound according to claim 7, represented by the following formula (IV):



(wherein R^1 and R^2 have the same meanings as defined in claim 7 [above]), a pharmacologically acceptable salt thereof or hydrates thereof.

13. (Amended) A pharmaceutical composition comprising a pharmacologically acceptable amount of the compound represented by the following formula (I), a pharmaceutically acceptable salt thereof or hydrates thereof, and pharmacologically acceptable carriers:

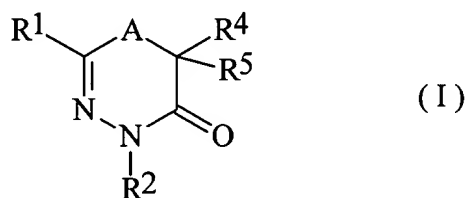


wherein A represents oxygen, sulfur or a group represented by the formula $>NR^3$ (wherein R^3 represents hydrogen atom or a lower alkyl group); R^1 and R^2 are the same as or different from each other and each represents an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed

from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group, an optionally substituted heteroaryl alkyl group, an optionally substituted aryl alkenyl group, an optionally substituted heteroaryl alkenyl group, an optionally substituted piperidyl group, an optionally substituted piperazinyl group, a morpholinyl group, an optionally substituted lower C_{3-8} cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an adamantyl group, an optionally substituted amino group or an optionally substituted amide group that is $CO-N(R_a)R_b$, wherein R_a and R_b are hydrogen and C_{1-6} alkyl group; and R^4 and R^5 are the same as or different from each other and each represents hydrogen atom, hydroxyl group, halogen atom, nitrile group, nitro group, a lower alkyl group, an aryl group or a heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms provided that A is an oxygen atom, when R^1 and R^2 are both phenyl; and when A is a sulfur atom, R^1 is an aryl which may have a substituent, a heteroaryl which may have a substituent that is formed from one or two 5-6 membered rings that may contain 1-4 heteroatoms, an aralkyl which may have a substituent, a heteroarylalkyl which may have a substituent

an arylalkenyl which may have a substituent,
a heteroarylalkenyl which may have a substituent,
a piperidyl which may have a substituent,
a piperadiny1 which may have a substituent,
a morpholinyl which may have a substituent,
a lower C₃₋₈ cycloalkyl which may have a substituent,
tetrahydrofuranyl,
adamantyl or
an optionally substituted amide, that is -CO-N(R_a)R_b, wherein R_a
and R_b are hydrogen and C₁₋₆ alkyl group.

15. (Amended) A pharmaceutical preparation comprising the compound represented by the following formula (I), a pharmaceutically acceptable salt thereof or hydrates thereof:



wherein A represents oxygen, sulfur or a group represented by the formula $>NR^3$ (wherein R^3 represents hydrogen atom or a lower alkyl group); R^1 and R^2 are the same as or different from each other and each represents an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed from one or two 5-6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group, an optionally substituted heteroaryl alkyl group, an optionally substituted aryl alkenyl group, an optionally substituted heteroaryl alkenyl group, an optionally substituted piperidyl group, an optionally substituted piperazinyl group, a morpholinyl group, an optionally substituted lower C_{3-8} cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an adamantyl group, an optionally substituted amino group or an optionally substituted amide group that is $-CO-N(R_a)R_b$, wherein R_a and R_b are hydrogen or C_{1-6} alkyl group; and R^4 and R^5 are the same as or different from each other and each represents hydrogen atom, hydroxyl group, a halogen atom, nitrile group, nitro group, a lower alkyl group, an aryl group or a heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms provided that A is an oxygen atom, when R^1 and R^2 are both phenyl; and

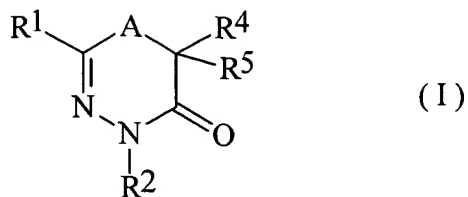
when A is a sulfur atom, R¹ is
an aryl which may have a substituent,
a heteroaryl which may have a substituent that is formed from
one or two 5-6 membered rings that may contain 1-4 heteroatoms,
an aralkyl which may have a substituent,
a heteroarylalkyl which may have a substituent,
an arylalkenyl which may have a substituent,
a heteroarylalkenyl which may have a substituent,
a piperidyl which may have a substituent,
a piperadinyll which may have a substituent,
a morpholinyl which may have a substituent,
a lower C₃₋₈ cycloalkyl which may have a substituent,
tetrahydrofuranyl,
adamantyl or
an optionally substituted amide, that is -CO-N(R_a)R_b, wherein R_a
and R_b are hydrogen and C₁₋₆ alkyl group.

24. (Amended) A method of [preventing,] treating and ameliorating nerve degeneration diseases, which comprises administering a pharmacologically effective amount of the pharmaceutical preparation according to claim 15 or 16 to a patient.

25. (Amended) A method of [preventing,] treating and ameliorating demyelinating nerve diseases, which comprises administering a pharmacologically effective amount of the pharmaceutical preparation according to claim 15 or 16 to a patient.

26. (Amended) A method of [preventing,] treating and ameliorating acute nerve degeneration after cerebral ischemia, traumas in the head and spinal injuries, Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, Huntington's chorea, epilepsy, pain, multiple sclerosis, encephalomyelitis, Guillain Barre syndrome, Marchiafava Bignami disease, Devic disease, Balo disease, HIV or HTLV myelopathy or leukoencephalopathy, which comprises administering a pharmacologically effective amount of the pharmaceutical preparation according to claim 15 or 16 to a patient.

Claim 32. A compound represented by the following formula (I), a pharmacologically acceptable salt thereof or hydrates thereof:



wherein A represents oxygen, sulfur or a group represented by the formula $>NR^3$ (wherein R^3 represents hydrogen atom or a lower alkyl group); R^1 represents an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group, an optionally substituted heteroaryl alkyl group, an optionally substituted aryl alkenyl group, an optionally substituted heteroaryl alkenyl group, an optionally substituted piperidyl group, an optionally substituted piperazinyl group, a morpholinyl group, an optionally substituted lower C_{3-8} cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an adamantyl group, an optionally substituted amino group or an optionally substituted amide group that is $-CO-N(R_a)R_b$ wherein R_a and R_b are hydrogen and C_{1-6} alkyl group; R^2 represents an optionally substituted aryl group, an optionally substituted heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms, an optionally substituted aralkyl group wherein it is not benzyl, an

optionally substituted heteroarylalkyl group wherein it is not pyrimidinyl alkyl, an optionally substituted aryl alkenyl group, an optionally substituted heteroaryl alkenyl group, an optionally substituted piperidyl group, an optionally substituted piperazinyl group, a morpholinyl group, an optionally substituted lower C_{3-8} cycloalkyl group, a tetrahydrofuranyl group, a tetrahydropyranyl group, an adamantyl group, an optionally substituted amino group or an optionally substituted amide group that is $-CO-N(R_a)R_b$, wherein R_a and R_b are hydrogen and C_{1-6} alkyl group; and R^4 and R^5 are the same as or different from each other and each represents hydrogen atom, hydroxyl group, nitrile group, nitro group, a lower alkyl group, an aryl group or a heteroaryl group that is formed from one or two 5 or 6 membered rings that may contain from 1 to 4 heteroatoms,

provided that A is an oxygen atom, when R^1 and R^2 are both phenyl; and

when A is a sulfur atom, R^1 is

an aryl which may have a substituent,

a heteroaryl which may have a substituent that is formed from one or two 5-6 membered rings that may contain 1-4 heteroatoms,

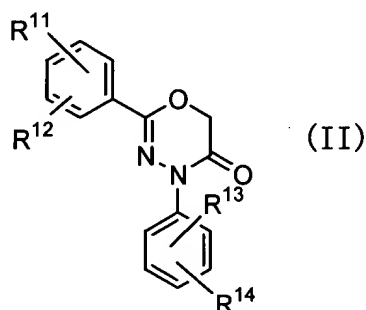
an aralkyl which may have a substituent,

a heteroarylalkyl which may have a substituent,

an arylalkenyl which may have a substituent,

a heteroarylalkenyl which may have a substituent,
a piperidyl which may have a substituent,
a piperadiny1 which may have a substituent,
a morpholinyl which may have a substituent,
a lower C₃₋₈ cycloalkyl which may have a substituent,
tetrahydrofuranyl,
adamantyl or
an optionally substituted amide, that is -CO-N(Ra)Rb, wherein Ra
and Rb are hydrogen and C₁₋₆ alkyl group; and

provided that the compounds represented by the following
 formula (II):



(wherein R¹¹ and R¹² are the same as or different from each other
 and each represents hydrogen atom, fluorine, chlorine, bromine,
 iodine, a C1-C2 fluoroalkyl group, a C1-C2 chloroalkyl group, a
 C1-C2 bromoalkyl group, a C1-C6 alkyl group, a C3-C6 cycloalkyl
 group, a C7-C9 aralkyl group, phenyl group, a C1-C6 alkoxy
 group, a C1-C6 alkylthio group, a C1-C6 alkylsulfinyl group, a
 C7-C9 aralkoxy group, phenoxy group, phenylthio group,
 phenylsulfonyl group, an alkali metal carboxylate C2-C5

alkoxycarbonyl group or a group represented by the formula -
 $N(R^{15})R^{16}$ (wherein R^{15} and R^{16} are the same as or different from
each other and each represents hydrogen atom or a C1-C2 alkyl
group); and R^{13} and R^{14} are the same as or different from each
other and each represents a C₁₋₄ alkylsulfonyl group, nitro
group, a group represented by the formula $-OCH_nX_{3-n}$ (wherein X
represents fluorine, chlorine, bromine or iodine; and n is an
integer of 1 to 3) or the same groups as defined above for R^{11}
and R^{12}) are excluded.

Claim 33 is added.